

# Melanosis Coli

Suharno\*, Putut Bayupurnama\*\*, Neneng Ratnasari\*\*

\*Department of Internal Medicine, Margono Soekarjo General Hospital, Purwokerto

\*\* Division of Gastroenterology and Hepatology, Department of Internal Medicine, Faculty of Medicine, Gadjah Mada University/Dr. Sardjito General Hospital, Yogyakarta

## Corresponding author:

Putut Bayupurnama. Division of Gastroenterology and Hepatology, Department of Internal Medicine, Dr. Sardjito General Hospital. Jl. Kesehatan No. 1 Yogyakarta Indonesia. Phone: +62-274-553119; Facsimile: +62-274-553120. E-mail: pututby@yahoo.com

## ABSTRACT

*Melanosis coli is a brownish discoloration of the colonic mucosa caused by the accumulation of pigment in macrophages of the lamina propria. We reported a 62 years old woman with prolonged constipation since 10 years ago. She underwent haemorrhoidectomy when 17 years old. Since 4 years ago she regularly consumed herbal laxative. On 27 January 2015 underwent colonoscopy at Sardjito hospital Yogyakarta. Colonoscopic examination revealed Melanosis coli.*

**Keywords:** *Melanosis coli, herbal laxative*

## ABSTRAK

*Melanosis Coli adalah kelainan mukosa usus berwarna kecoklatan karena timbunan pigmen di makrofag lamina propria. Kami melaporkan seorang wanita 62 tahun dengan keluhan utama konstipasi sejak 10 tahun yang lalu. Dia pernah menjalani operasi haemoroidektomi pada usia 17 tahun. Sejak 4 tahun yang lalu rutin mengkonsumsi jamu pencahar herbal untuk memudahkan buang air besar. Pada pemeriksaan kolonoskopi tanggal 27 Januari 2015 di rumah sakit Dr. Sardjito Yogyakarta didapatkan gambaran Melanosis coli.*

**Kata kunci:** *Melanosis coli, pencahar herbal*

## INTRODUCTION

Melanosis coli first described in 1835 by Billiard and named by Virchow in 1857, melanos coli is characterized by a brown to black pigmentation of colonic mucosa that is associated with chronic laxative use. It is typically found in patients who chronically use anthranoid laxatives such as sennosides, cascara frangula, rhubarb, and aloe but may be seen in patients who do not use laxative and suffer constipation. A study of melanos coli in patients with underlying irritable bowel disease, however, only 20% admitted to use laxative.<sup>1</sup>

Melanos coli develops in over 70% of persons who use long term anthraquinone laxatives often within 4 months of use with average 9 month. There

is an earlier age of onset in the females, with a higher detection rate. Long-term use is generally believed to be necessary to cause melanos coli. The condition is widely regarded as benign and reversible, and disappearance of the pigment generally occurs within a year of stopping laxatives.<sup>2</sup>

The condition has no specific symptom on its own. It is a fairly frequent incidental finding of colonic biopsies and resection specimens. The pigmentation is caused by apoptotic cells which are ingested by macrophages and subsequently transported into the lamina propria, where lysosomes use them to produce lipofuscin pigment, not melanin as the name suggests. The pigment proved to be more

characteristic of lipofuscin, both histochemically and ultrastructurally.<sup>3,4</sup>

### CASE ILLUSTRATION

A 62 year old woman with prolonged constipation since 10 years ago, underwent haemorrhoidectomy when 17 years old. Since 4 years ago she consumed laxative herbal. She consumed it three times a day. The condition of feces after consuming laxative herbal is normal. On 27 January 2015 underwent colonoscopy at Sardjito hospital Yogyakarta. Colonoscopy examination results revealed melanosis coli. Physical examination showed no abnormality. Laboratory examination showed normal values.

### DISCUSSION

Chronic constipation is an important component of clinical gastroenterology practice worldwide. Based on the definition, either self-reported or using Rome criteria, chronic constipation can affect from 2-27% of the population. Constipation is physically and mentally troublesome for many patients, and can significantly interfere with their daily living and well-being. Although only a proportion of patients with constipation seek medical care, most of them use prescribed or over-the-counter medication to improve their condition. The health care costs of constipation are significant as evidenced by the hundreds of million dollars spent yearly on laxatives alone. Because constipation is more common in older patients and life expectancy is increasing, an increase in the prevalence of constipation is expected in the years to come, with the associated impact on quality of life and socioeconomic burden.<sup>5</sup>

Anthraquinone containing laxatives are frequently used for chronic constipation. Anthraquinone compounds are present in many over-the-counter laxatives, including herbal medicines. In addition, laxatives are frequently used as slimming agents. With sufficient dose and duration of laxative ingestion, melanosis coli can develop in as short as 6 weeks.<sup>6</sup>

Anthranoid-containing herbal laxatives damage epithelial cells, leading to changes in absorption, secretion, and motility. They can induce cell loss, shortening of mucosal crypts and increased cell proliferation.<sup>7</sup> Upon ingestion of anthraquinone containing herbs, an active derivative, rhein, is formed in the large intestine by bacteria, which causes injury to the cells in the lining of the intestine and leads to apoptosis. These cells are either shed into the colonic

lumen, or the damaged organelles are sequestered in autolysosomes in macrophages where digestion to residual lipofuscin bodies results. When sufficient cells have been damaged, the distinctive pigmentation of the bowel mucosa develops.<sup>8,9</sup>

The pigment distribution is seen mainly in cecum and proximal colon. The primary pathologic finding is increased macrophages in the lamina propria and muscularis mucosa with lipofuscin pigment. The pigmentation is triggered by deposits of apoptotic cells, which are ingested by adjacent macrophages within the epithelial tissue. These macrophages migrate in the lamina propria, where lysosomes convert the remains of the cells into lipofuscin pigment. Thus, the term melanosis may be misleading, since the pigment is not melanin.<sup>10</sup>

Melanosis coli is most often detected during examination for longstanding constipation, often in conjunction with a history of chronic use of anthracene cathartics (including cascara, senna, aloes and rhubarb).<sup>11,12</sup>

In this case, patient consumed rhubarb-containing laxative daily for 4 years to overcome constipation. Rhubarb (*Rhein radix*) contains a complex mixture of different hydroxanthracene derivatives. The amount is 3-12% depending on the method of determination. These hydroxanthracene derivatives mainly (60-80%) consist of mono- and diglycosides of 1,8-dihydroxyanthrachinons aloemodin, chrysophanol, emodin, physcion and rhein, and only small amounts of the respective aglycones. Dianthrone glycosides (sennosides) are also present (10-25%).<sup>13</sup>

Recent experimental and clinic studies have revealed some proofs of laxative abuse-melanosis coli and colorectal carcinoma relationship, but the topic is still quite speculative. Siegers et al have reported the relation between melanosis coli and the increased rate of colorectal cancer, in a prospective study. They reported the rate of melanosis coli as: 6.9% in patients with normal endoscopy; 9.8% in patients with adenoma and 18.6% in patients with colorectal carcinoma.<sup>14</sup>

A prospective case control study performed by Nusko et al at the University of Erlangen to investigate the risk of anthranoid laxative use for the development of colorectal adenomas or carcinomas. A total of 202 patients with newly diagnosed colorectal carcinomas, 114 patients with adenomatous polyps, and 238 patients (controls) with no colorectal neoplasms who had been referred for total colonoscopy were studied. The use of anthranoid preparations was assessed by standardised interview, and endoscopically visible or microscopic melanosis coli was studied by histopathological

examination. No statistically significant risk of anthranoid use for the development of colorectal adenomas (unadjusted OR = 1.0; 95% CI: 0.5–1.9) or carcinomas (unadjusted OR = 1.0; 95% CI: 0.6–1.8). Even after adjustment for the risk factors age, sex, and blood in the stools by logistic regression analysis the OR for adenomas was 0.84 (95% CI: 0.4–1.7) and for carcinomas 0.93 (95% CI: 0.5–1.7). Also, there were no differences between the patient and control groups for duration of intake. Macroscopic and high grade microscopic melanosis coli were not significant risk factors for the development of adenomas or carcinomas. Neither anthranoid laxative use, even in the long term, nor macroscopic or marked microscopic melanosis coli were associated with any significant risk for the development of colorectal adenoma or carcinoma.<sup>15</sup>

The use of complementary and alternative medicine (CAM) has been on the rise in the past few decades. CAM use appears to be more common among those with functional bowel disorders. Patients with chronic and refractory gastrointestinal disorders tend to use CAM more frequently: herbal products being the most commonly used. Overall, 10% of herbal therapy is used for digestive symptoms. Indeed, up to 30% of patients with chronic liver disease and 40% of patients with irritable bowel syndrome claim to have used some form of herbal medication. An estimated 51% of patients with gastrointestinal disorders have tried some form of

CAM.<sup>16</sup> This situation also the as the same in Indonesia.

Although melanosis coli is a harmless discoloration of colonic mucosa resulting from complementary or alternative medicine, it is believed that this association with herbals was often overlooked, not suspected by patients nor enquired by doctors. Therefore, it should be emphasized to patients that “natural” or “alternative” is not equal to “safe” or “without unwanted consequences”.<sup>17</sup>

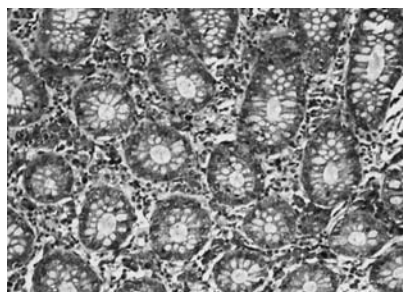
No medical treatment is necessary for melanosis coli. The condition is benign and reversible. Disappearance of the pigment generally occurs within a year after a patient stops taking anthraquinone.<sup>10</sup>

## REFERENCES

1. Pardi DS, Tremeini WJ, Rothernberg HJ, Batts KP. *Melanosis coli* in inflammatory bowel disease. *J Clin Gastroenterol* 1998;26:167-70.
2. Siang-Tong Kew. *Melanosis Coli* *JeSME* 2012;6:S53-60.
3. Ghadially FN, Parry E. An electron-microscope and histochemical study of melanosis coli. *J Pathol Bacteriol* 1966;92:313-17.
4. Ghadially FN. Lysosomes, Ultrastructural pathology of the cell and matrix. 2<sup>nd</sup> ed. London, Butterworths 1982. pp.435-579.
5. Higgins PD, Johanson JF. Epidemiology of constipation in North America: a systematic review. *Am J Gastroenterol* 2004;99:750-9.
6. Kav, Taylan, Bayraktar, Yusuf. Herbal remedies are the main etiologic factor in melanosis coli, a case series study. *Central European J Med* 2010;5:347-53.
7. Gorkom BAP van, Vries EGE de, Karrenbeld A, Kleibeuker JH. Anthranoid laxatives and their potential carcinogenic effects. *Aliment Pharmacol Ther* 1999;13:443-52.
8. Muller-Lissner SA Adverse effects of laxatives: fact and fiction. *Pharmacology* 1993;47:138-45.
9. De WP. Metabolism and Pharmacokinetics of Anthranoids. *Pharmacology* 1993;47:86-97.
10. S Chatni, H Peshwe. *Melanosis coli*. *Japi* 2006;58:548.
11. Badiali D, Marcheggiano A, Pallone F, Paoluzi P, Bausano G: *Melanosis of the rectum in patients with chronic constipation*. *Dis Colon Rectum* 1985;28:241-5.
12. Ewing CA, Lalan M, Chucker F, Ozdemirli M. *Melanosis coli* involving pericolic lymph nodes associated with the herbal laxative Swiss Kriss: a rare and incidental finding in a patient with colonic adenocarcinoma. *Arch Pathol Lab Med* 2004;128:565-7.
13. European Medicines Agency. Assessment report for Rhubarb (*Rheiradix*), London [serial online] 2008 [cited 2016 June 1]. Available from: URL: <http://www.ema.europa.eu>
14. Siegers CP, von Hertzberg-Lottin E, Otte M. Anthranoid laxative abuse-a risk for colorectal cancer? *Gut* 1993;34:1099-101.
15. Nusko G, Schneider B, Ernst H. *Melanosis coli* - a harmless pigmentation or a precancerous condition? *Z Gastroenterol* 1997;35:313-8.
16. Kirsten Tillisch. Complementary and alternative medicine for gastrointestinal disorders. *Clin Med* 2007;7:224-7.
17. Kunkel J, Schmidt S, Loddenkemper C, Zeitl M, Schulzke JD. Chronic diarrhea and melanosis coli caused by wellness drink. *Interna J Colorectal Dis* 2009;24:595-6.



**Figure 1.** Colonoscopic examination, melanosis coli, Leopard skin pattern



**Figure 2.** Histologic examination, brown pigment in lamina propria of colonic mucosa .